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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	7

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/628,225	W Bachovchin et al
Examiner	**Group Art Unit**
J. Russel	1653

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 7-28-2000.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-37 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-37 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The drawing(s) filed on 7-28-2000 is/are objected to by the Examiner.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

1. As originally filed, this application did not contain a claim numbered "17". Accordingly, claims which were originally numbered 18 through 38 have been re-numbered under 37 CFR 1.126 as 17 through 37, respectively. The dependencies of re-numbered claims 31-36 has been corrected in accordance with the above re-numbering. Any future reference to the claims will use their re-numbered claim numbers.

2. With respect to the declaration signed by Inventor Bachavchin filed May 11, 2001, the examiner assumes that the inventor's post office address is the same as his residence address. If this is incorrect, Applicant is required by 37 CFR 1.33(a) to provide a statement over applicant's signature providing a complete post office address.

3. The drawings are objected to because in the heading to Figure 3, "Pro(boro)pro" is misspelled. Correction is required.

Applicant is required to submit a proposed drawing correction in response to this Office action. Any proposal by Applicant for amendment of the drawings to cure defects must consist of two parts:

a) A separate letter to the Draftsperson in accordance with MPEP 608.02(r); and

b) A print or pen-and-ink sketch showing changes in red ink or with the changes otherwise highlighted in accordance with MPEP 608.02(v).

IMPORTANT NOTE: The filing of new formal drawings to correct the noted defect(s) may be deferred until the application is allowed by the examiner, but the print or pen-and-ink sketch with proposed corrections shown in red ink or with the changes otherwise highlighted is required in response to this Office action, and may not be deferred.

4. The abstract of the disclosure is objected to because it is insufficiently detailed as to the identity of the active agents which are to be used. Correction is required by submission of a new abstract on a separate sheet of paper. See MPEP § 608.01(b).

5. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 and/or 120 as follows:

The claim for priority inserted by the preliminary amendment filed July 28, 2000 is objected to because it does not indicate what type of priority is being claimed. For example, the claim for priority does not use the "claims the benefit of" language which is indicative of a claim for priority under 35 U.S.C. 119(e), and does not use the "is a continuation of" language which is indicative of a claim for priority under 35 U.S.C. 120. The claim for priority inserted by the preliminary amendment filed July 28, 2000 is objected to because there is no copendency between either the U.S. Provisional Application or the PCT Application and the instant application. Note that the declaration indicates that a claim for priority under 35 U.S.C. 119 is intended, but both the U.S. Provisional Application and the PCT Application were filed more than one year prior to the filing date of the instant application. Finally, the claim for priority inserted by the preliminary amendment filed July 28, 2000 is objected to because it is not the first sentence of the specification. See MPEP 310.

Correction is required.

6. The disclosure is objected to because of the following informalities: At page 9, line 6, "organics" is misspelled. At page 18, line 6, "halogenated" is misspelled. At page 18, line 10, "lik." should be changed to "like". Appropriate correction is required.

7. Claims 15-28 and 31-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. There is no antecedent basis in the claims for the phrase "the Cα carbon" at claim 15, line 5. The claim does not previously mention a Cα carbon, and the formula does not inherently require a Cα carbon because in the formula, Z can be N. At claim 15, page 54, lines 9-10 and 15-16, and claim 28, lines 12-13, the "such as" phrases are indefinite because it is not clear if the scope of the claims is to be limited to the particularly exemplified substituents or not. It is suggested that the "such as" phrases could be deleted and made the subject matter of further dependent claims. Claim 15 is indefinite because it defines a variable X at page 54, line 14, which is not used in any of the chemical structures. It is possible that Applicants intended "Z" instead of "X". At claim 16, page 55, line 1, and claim 28, line 6, the first chemical structure is indefinite because it includes a monovalent oxygen atom At claim 16, page 55, lines 9-11; claim 28, page 61, lines 5-7; and claim 31, page 63, lines 13-14; the "including" and the "such as" phrases are indefinite because it is not clear if the scope of the claims is to be limited to the exemplified and/or particularly exemplified substituents or not. It is suggested that the "including" and the "such as" phrases could be deleted and made the subject matter of further dependent claims. At claim 16, page 55, lines 10-11; claim 28, page 61, lines 6-7; and claim 31, page 63, line 14; the phrase "or the like" is indefinite because it is not clear what degree of structural and/or functional similarity a chemical substituent must have with pinacol in order to be considered "like" pinacol. Claims 20 and 21 are indefinite because they indicate that R2 and R3 can be small hydrophobic groups. However, claim 15, upon which claims 20 and 21 ultimately depend, does not recite "small hydrophobic groups" as possibilities

for R2 or R3, and the correspondence is not clear between the small hydrophobic groups of claims 20 and 21 and the substituents recited in the definitions of R2 and R3 in claim 15. The general formula in claim 28 appears to be incorrect given the definition of R_1 set forth in the claim. The definition of R_1 indicates that, e.g., C-terminally-linked amino acid residues and amino protecting groups are permitted. However, as shown in the general formula, R_1 is not bonded to an amino group. At claim 28, line 6, the "as for example" phrase is indefinite because it is not clear if W is to be limited to the specific functional groups or not. It is suggested that the phrase could be deleted and made the subject matter of a further dependent claim. In any event, the phrase appears to be redundant to the requirements set forth in the definition of W in claim 16, upon which claim 28 depends. At claim 31, page 62, lines 10-11 and 17-18, the "such as" phrases are indefinite because it is not clear if the scope of the claim is to be limited to the particularly exemplified substituents or not. It is suggested that the "such as" phrases could be deleted and made the subject matter of further dependent claims. Claim 31 is indefinite because it defines variables R_5 and R_{61} which are not used in any of the chemical structures found in the claim. The variable R'_7 at claim 31, page 62, line 26, is not defined in the claim. The variable R_{62} at claim 31, page 62, line 4, is not defined in the claim. At claim 31, page 63, lines 10-11, the "preferably" and the "more preferably" phrases are indefinite because it is not clear if the variables are to be limited to the preferred or to the more preferred substituents or not. It is suggested that the claims could be deleted and made the subject matter of further dependent claims. Claim 37 is indefinite because it is not clear what constitutes a boronyl inhibitor of a peptidomimetic. It is not clear what peptidomimetic is to be inhibited.

8. Claims 4-7, 13, 15, 16-28, and 30-36 are objected to because of the following informalities: At claim 4, line 2, "of" should be inserted after "inhibitors". At claim 5, "the" should be inserted before "dipeptidylpeptidase". At claim 6, "the" should be inserted before "protease". At claim 7, line 3, and claim 32, line 3, a conjunction, e.g., "or" or "and", should be inserted before "hyperlipoproteinemia". At claim 13, line 1, "weights" should be changed to "weight". In the general formula at claim 15, line 3, subscripts are not used in the substituents R1, R2 and R3; however, in the definitions of these substituents (see, e.g., page 54, lines 4, 7, and 14), subscripts are used. Claims 15, 16, and 18-28, and 31 should be reviewed to ensure that claim terminology is standardized. At claim 15, page 54, lines 6, 13, and 20, and claim 28, lines 10, 16, and 20, "or" should be inserted before the last chemical structure in the line. At claim 15, page 54, line 21, and claim 28, line 21, "a" (second, third, and fourth occurrences) should be changed to "an". At claim 15, page 54, line 23, and claim 28, line 23, "or" should be inserted after the last comma in the line. At claim 16, page 55, line 5, "or" should be inserted before the last chemical structure in the line. At claim 16, page 55, line 16, and claim 28, page 61, line 12, a semicolon should be inserted at the end of the line. Claims 16 and 19 do not end with periods. At claim 22, "halogenated" is misspelled. At claim 24, line 5, and page 57, line 11, "or" should be inserted before the last chemical structure in each line. At claim 24, line 5, "C-" should be inserted before "terminally", and at line 6, "C-" should be deleted. At claim 24, page 57, line 1 (second, third, and fourth occurrences) and line 14 (first occurrence), "a" should be changed to "an". At claim 24, page 57, line 7, a semicolon should be inserted at the end of the line. Claims 25 and 26 contain the same informalities as does claim 24. At claim 28, line 7, a semicolon should be inserted at the end of the line. At claim 28, page 61, line 3, "independently" is

misspelled. At claim 30, line 2, "a" should be inserted after "including". At claim 31, page 62, lines 14, 21, and 26, and page 63, line 9, "or" should be inserted before the last chemical structure in the line. At claim 31, page 63, line 1, "a" (second, third, and fourth occurrences) should be changed to "an". At claim 31, page 63, line 3, "or" should be inserted after the last comma in the line. Appropriate correction is required.

9. Claims 22, 24-26, and 28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 22 recites that R5 can be a halogenated lower alkyl, which is not a possibility embraced by the definition of R5 in claim 16. Claim 24 recites possibilities for R_6 at page 57, lines 6 and 7, which are not embraced by the definition of R_6 in claim 15, upon which claim 24 ultimately depends. Claims 25 and 26 do not further limit claim 15 for the same reason that claim 24 does not further limit claim 15. In addition, the definition of X_1 in claim 26 indicating that the substituent can be hydrogen is not embraced by the definition of X_1 in claim 16. Claim 28 does not further limit claim 16 because the inhibitor having the general formula recited in claim 28 does not comprise the 4-8 membered heterocycle required by claim 16.

10. Applicants should check their definition of R_3 when X is N (see claim 15, page 54, line 15) to determine whether or not they intend to recite a compound comprising a tetravalent nitrogen atom. Applicants should check their definitions of R_{51} (see claim 16, page 55, line 13, and claim 28, page 61, line 9) to determine whether or not they intend to recite a compound

comprising a trivalent sulfur atom. In general, the claims would benefit from substantial revision.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v.

Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

12. Claims 1, 3, 5-10, 12, 13, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by the Deacon et al article. The Deacon et al article teaches potentiating the insulinotropic effect of GLP-1 by administering a DPIV inhibitor, valine-pyrrolidide. Administration is in vivo to a pig, and results in reduced proteolysis of GLP-1, reduced blood glucose, and increased glucose tolerance. See, e.g., the Abstract; Figure 1; and page 768, column 1. With respect to instant claims 8-10, in view of the similarity in structure and function between the DPIV inhibitor of the Deacon et al article and Applicants' claimed DPIV inhibitor, the EC50's and Ki for the DPIV inhibitor of the Deacon et al article will inherently be the same as is recited in instant claims 8-10. Sufficient evidence of similarity is deemed to be present between the DPIV inhibitor of the Deacon et al article and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitor of the Deacon et al article. With respect to instant claim 29, because the same inhibitor is being administered to the same animal in the same amounts in the method of the Deacon et al article as in Applicants' claimed method, inherently metabolism of the same peptide hormones will be modified to the same extent in the method of the Deacon et al article as is claimed by Applicants.

13. Claims 1-3, 5-16, 20, 21, 25, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '309. The WO Patent Application '309 teaches administering DPIV inhibitors to treat human disease. The inhibitors are highly potent, with Ki

values ranging into the nanomolar range or less, and are chemically stable. The DPIV inhibitors with the smallest Ki have the same structure as is set forth in Applicants' claims 15, 16, 20, 21, and 25. See, e.g., page 3, lines 10-21; page 4, lines 1-3; compounds 23, 38-40 and 97; and Table 9. Because the same active agents are being administered to the same animals according to the same method steps, inherently metabolism of GLP-1, glucose metabolism, insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, hyperlipoproteinemia, and peptide hormone metabolism will be modified to the same extent in the method of the WO Patent Application '309 as is claimed by Applicants. With respect to instant claims 8-10, in view of the similarity in structure and function between the DPIV inhibitor of the WO Patent Application '309 and Applicants' claimed DPIV inhibitor, the EC50's and Ki for the DPIV inhibitor of the WO Patent Application '309 will inherently be the same as is recited in instant claims 8-10. Sufficient evidence of similarity is deemed to be present between the DPIV inhibitor of the WO Patent Application '309 and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitors of the WO Patent Application '309. With respect to instant claim 14, because of the similarity in structure between the DPIV inhibitors of the WO Patent Application '309 and those recited in Applicants' claims, the DPIV inhibitors of the WO Patent Application '309 would have been expected to be orally active to the same extent claimed by Applicants. Note that while instant claim 14 recites a property of the DPIV inhibitors to be administered, it does not actually recite a positive process step in which the inhibitors are administered orally.

14. Claims 2, 11, 14-16, 20, 21, and 25 are rejected under 5 U.S.C. 103(a) as being obvious over the Deacon et al article as applied against claims 1, 3, 5-10, 12, 13, and 29 above, and further in view of the WO Patent Application '309. The Deacon et al article does not disclose the use of DPIV inhibitors having a Ki as recited in instant claims 2 and 11, having oral activity, or having the structure recited in instant claims 15, 16, 20, 21, and 25. Application of the WO Patent Application '309 is the same as in the above rejection of claims 1-3, 5-16, 20, 21, 25, and 29. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the DPIV inhibitors of the WO Patent Application '309 in the method of the Deacon et al article because the DPIV inhibitors of the WO Patent Application '309 have the advantage of having a low Ki and of having chemical stability, which would permit the use of smaller dosages of the active agent, because the DPIV inhibitors of the WO Patent Application '309 are described as being generally useful as inhibitors of DPIV-mediated processes (see, e.g., the Abstract), and because the method of the Deacon et al article operates via a DPIV-mediated process.

15. Claims 1-3, 5-24, 26, 27, and 29-37 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '259. The WO Patent Application '259 teaches inhibiting the enzymatic activity of DPIV in a mammal by administering a peptide compound. The peptides compounds are proteolyzed by DPIV in vivo until a C-terminal dipeptide portion remains, which acts as an inhibitor of DPIV. The peptide compound is more stable in vivo than the C-terminal dipeptide portion. If the C-terminal dipeptide portion is chosen to be a dipeptide prolyl-boronic acid, then a potent and highly specific inhibitor having a Ki in the nanomolar range is ultimately released in vivo. Tetrapeptides comprising Ala-boroPro and Pro-boroPro as

the C-terminal dipeptide portions are taught. As an alternative to the boroPro group, trifluoroalkyl ketone groups are taught. See, e.g., page 2, lines 15-32; page 3, line 1 - page 7, line 16; page 14, lines 10-12; and page 14, line 34 - page 15, line 16. Because the same active agents are being administered to the same animals according to the same method steps, inherently metabolism of GLP-1, glucose metabolism, insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, hyperlipoproteinemia, and peptide hormone metabolism will be modified to the same extent in the method of the WO Patent Application '259 as is claimed by Applicants. With respect to instant claims 8-11 and 33-35, in view of the similarity in structure and function between the DPIV inhibitors of the WO Patent Application '259 and Applicants' claimed DPIV inhibitors, the EC50's and Ki's for the DPIV inhibitors of the WO Patent Application '259 will inherently be the same as is recited in instant claims 8-11 and 33-35. Sufficient evidence of similarity is deemed to be present between the DPIV inhibitors of the WO Patent Application '259 and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitors of the WO Patent Application '259. With respect to instant claims 14 and 36, because of the similarity in structure between the DPIV inhibitors of the WO Patent Application '259 and those recited in Applicants' claims, the DPIV inhibitors of the WO Patent Application '259 would have been expected to be orally active to the same extent claimed by Applicants. Note that while instant claims 14 and 36 recite a property of the DPIV inhibitors to be administered, they do not actually recite a positive process step in which the inhibitors are administered orally.

16. Claims 2, 11, 14-24, 26, 27, and 29-37 are rejected under 5 U.S.C. 103(a) as being obvious over the Deacon et al article as applied against claims 1, 3, 5-10, 12, 13, and 29 above, and further in view of the WO Patent Application '259. The Deacon et al article does not disclose the use of DPIV inhibitors having a Ki as recited in instant claims 2 and 11, having oral activity, or having the structure recited in instant claims 15-24, 26, 27, and 31. Application of the WO Patent Application '259 is the same as in the above rejection of claims 1-3, 5-24, 26, 27, and 29-37. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the DPIV inhibitors of the WO Patent Application '259 in the method of the Deacon et al article because the DPIV inhibitors of the WO Patent Application '259 have the advantage of having a low Ki and of having chemical stability, which would permit the use of smaller dosages of the active agent, because the DPIV inhibitors of the WO Patent Application '259 are described as being generally useful as inhibitors of DPIV-mediated processes (see, e.g., page 6, lines 4-10), and because the method of the Deacon et al article operates via a DPIV-mediated process.

17. Claim 4 is rejected under 35 U.S.C. 103(a) as being obvious over the Deacon et al article as applied against claims 1, 3, 5-10, 12, 13, and 29 above, and further in view of Efendic et al. The Deacon et al article teaches administration of GLP-1 in combination with a DPIV inhibitor in pigs, which were chosen because of their resemblance to humans in terms of gastrointestinal physiology (see page 764, column 2, second full paragraph), and teaches that this may be a viable approach to the management of diabetes (see the Abstract), but does not explicitly teach co-administering GLP-1 and a DPIV inhibitor to treat Type II diabetes. Efendic et al teach the administration of GLP-1 in order to treat type II diabetes (see, e.g., column 2, lines 37-49, and

column 4, lines 47-67). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat Type II diabetes using the combination of GLP-1 and a DPIV inhibitor taught by the Deacon et al article to treat Type II diabetes, because the Deacon et al article discloses that this may be a viable approach to the management of diabetes, because the Deacon et al article's in vivo pig model is predictive of in vivo success in humans due to its resemblance to humans in terms of gastrointestinal physiology, and because Efendic et al confirm that GLP-1 is useful in the treatment of Type II diabetes.

18. Claims 1-3, 5-18, 20, 21, 24, and 29-37 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '644. The WO Patent Application '644 teaches administering GLP-2 in combination with a DPP IV inhibitor such as Pro(boro)Pro in order to promote the growth or small and/or large intestine tissue in a mammal. Treatment of diabetes mellitus is also mentioned. The DPP IV inhibitor prevents proteolysis of GLP-2. See, e.g., page 3, lines 20-32, page 7, lines 15-22; page 9, line 17 - page 10, line 4; page 17, line 32; and Example 6. Because the same active agents are being administered to the same animals according to the same method steps, inherently metabolism of GLP-1, glucose metabolism, insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, hyperlipoproteinemia, and peptide hormone metabolism will be modified to the same extent in the method of the WO Patent Application '644 as is claimed by Applicants. With respect to instant claims 2, 8-11, and 33-35, in view of the similarity in structure and function between the DPIV inhibitor of the WO Patent Application '644 and Applicants' claimed DPIV inhibitor, the EC50's and Ki for the DPIV inhibitor of the WO Patent Application '644 will inherently be the same as is recited in instant claims 2, 8-11, and 33-35. Sufficient evidence of

similarity is deemed to be present between the DPIV inhibitor of the WO Patent Application '644 and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitors of the WO Patent Application '644. With respect to instant claim 14 and 36, because of the similarity in structure between the DPIV inhibitors of the WO Patent Application '644 and those recited in Applicants' claims, the DPIV inhibitors of the WO Patent Application '644 would have been expected to be orally active to the same extent claimed by Applicants. Note that while instant claims 14 and 36 recite a property of the DPIV inhibitors to be administered, they do not actually recite a positive process step in which the inhibitors are administered orally.

19. Claims 1-17, 20, 21, and 29 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Villhauer. Villhauer teaches treating non-insulin-dependent diabetes, i.e. Type II diabetes, and increasing glucose tolerance by administering a DPIV inhibitor having the same structure as Applicants' claims 15-17, 20, and 21. The inhibitors improve early insulin response to oral glucose challenges. Oral administration of the inhibitors is taught. See, e.g., the Abstract; column 9, lines 48-65; and column 10, lines 28-42. With respect to instant claims 2 and 8-11, in view of the similarity in structure and function between the DPIV inhibitor of Villhauer and Applicants' claimed DPIV inhibitor, the EC50's and Ki for the DPIV inhibitors of Villhauer will inherently be the same as is recited in instant claims 2 and 8-11. Sufficient evidence of similarity is deemed to be present between the DPIV inhibitors of Villhauer and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitors of Villhauer. With respect to instant claim 29, because the same active agents are being administered to the same animals according to the same

method steps, inherently peptide hormone metabolism will be modified to the same extent in the method of Villhauer as is claimed by Applicants.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Christopher Low can be reached at (703) 308-2923. The fax number for Art Unit 1653 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 305-7401 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.

Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1653

JRussel

August 30, 2001